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Molecular folding induced nanogold aggregation

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ABSTRACT

Bisacridinedione-functionalized gold nanoparticles (bisADD-GNPs) were prepared and characterized. BisADD is a flexible acyclic moiety and a specific Ca^{2+} sensor. Signaling of the binding events is achieved by the cation-induced folding of the bisADD-GNPs and the resultant fluorescence enhancement and visual color change are attributed to the suppression of photoinduced electron transfer (PET) through space and nano-Au aggregation. The selective binding of Ca^{2+} is clear from steady state fluorescence and TEM techniques.

In recent years, surface functionalization of gold nanoparticles (AuNPs) has attracted growing attention owing to their tunable photophysical properties and various potential applications, including colorimetric nanosensors in the chemical and biological sciences.[1] The visual-sensing ability of AuNPs relies on changes in the surface plasmon resonance (SPR), which is dependent on the aggregation state, surface morphology, and so on.[1–3] Generally, the aggregation of AuNPs in solution through analyte-triggered interparticle cross-linking leads to a change in color from red to blue or purple, which is useful for observing molecular-recognition events.[4] This fundamental optical property of AuNPs has been intensively used for the development of nanoparticle probes for biological macromolecules.[2,4]AuNPs have also been successfully used for the development of molecular probes for small molecules of organic and inorganic analytes.

The synthesis of Ca^{2+}-specific sensors using the principle of PET was suggested by de Silva et al.[5,6] A variety of crown-ether and related macrocyclic-based chemosensors are known, while the non cyclic crown-ether-based chemosensors are relatively rare.[7,8] In the majority of chemosensors reported so far, the signaling of the binding event is achieved by electron transfer,[9–11]energy or charge transfer processes[12,13], and chromophore (excimer and exciton) interaction.[14,15] Recently, gold nanoparticles-based colorimetric detection has been devised for a variety of targets including metal ions,[16–20] DNA[21,22] and bacterial toxins.[23,24] The aggregation of chromophore-functionalized gold nanoparticles upon binding to a target results in a colorimetric response that is indicated by broadening and shifting of surface plasmon resonance peak.

Colorimetric methods are convenient and attractive because the color changes can be easily discerned with the naked eye. In a recent effort, Kim et al. and De la Fuente et al. synthesized calsequestrin and lactose-functionalized gold nanoparticles (GNPs) and used for Ca^{2+} detection.[25,26] We have already shown[27] that PET suppression results in fluorescence enhancement when acyclic polyether linked chromophore is folded with Ca^{2+}. In the present work, we have synthesized bisADD-GNP conjugate, which shows Ca^{2+}-induced folding of the bichromophore-GNPs resulting in the visual color change due to nano-Au aggregation with fluorescence enhancement due to the suppression of through space PET.

The synthetic procedure is shown in Scheme 1. Refluxing a mixture of tetraketone **1** and thioctic-hydrazide in acetic acid afforded the monoacridinedione derivative **2**. A mixture of **2**, pentaethylene glycol ditosylate and NaH in DMF (30 ml) on refluxing, afforded bisacridinedione derivative **3**; the crude product was recrystallized from a mixture (9:1) of $CHCl_3$ and methanol to yield a yellow powder of bisADD. In most of the literature, the synthesis of monolayer-protected clusters (MPCs) adopts modification of the method reported by Brust et al.; this procedure involves a two-phase (water-toluene) extraction of tetrachloro aurate ($AuCl_4^-$) using a phase-transfer reagent (TOAB), followed by reduction.[28] Addition of $NaBH_4$ to the mixture of **3** and $HAuCl_4$ in the presence of TOAB reduces the disulfide to thiol as well as enables the formation of metallic gold nuclei, which leads to the formation of S–Au bond[29] to produce **4**. (synthesis and characterization data are available in the SM).

The HR TEM image was recorded by drop-casting dilute suspension of **4** on a carbon-coated copper grid and the images are presented in Figure 1. Three-dimensional approach in TEM images indicates that bisADD is anchored on the surface of the gold nano-

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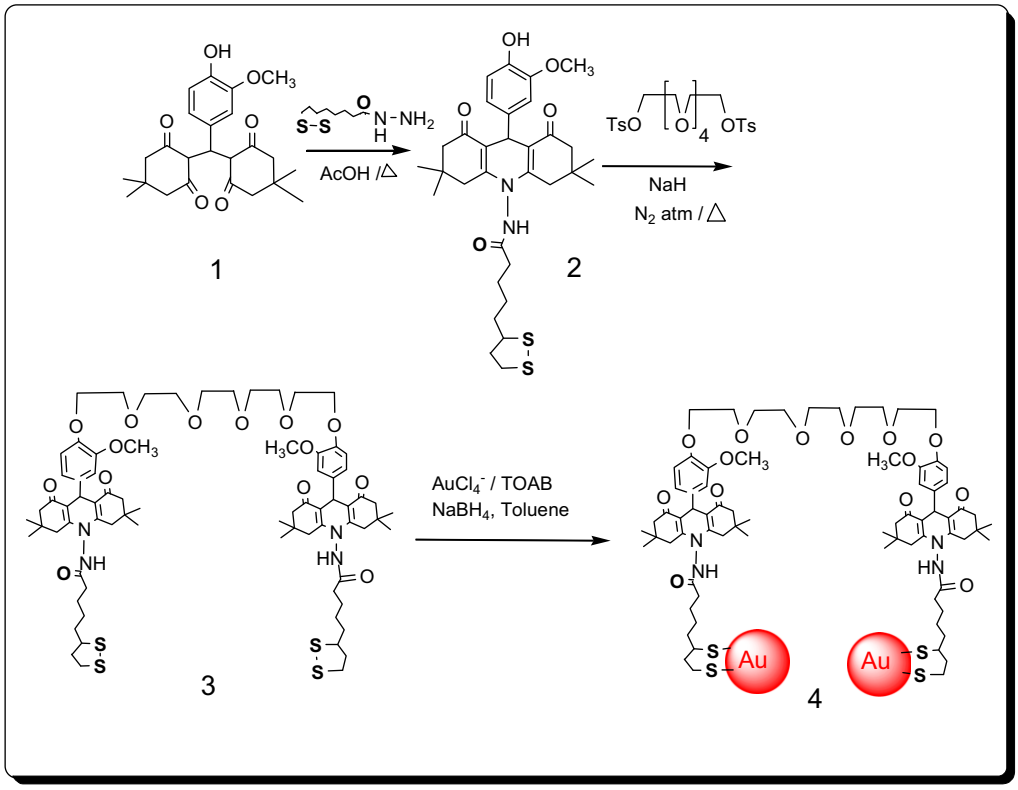


Scheme 1. Schematic illustration of synthesis and assembly of bisADD-GNPs via the reaction of $HAuCl_4$ with bisADD.

particles (GNPs). The size of GNPs was found to have an average diameter of 4.5 nm. When the bisADD molecules were functionalized on gold nanoparticles, it was found that approximately 97 bisADD molecules were bound to single nanoparticles if the foot print area of the dithiol molecule is 0.657 nm^2. Gold nanoparticles have a total surface area of 63.58 nm^2. When Ca^{2+} ions (0.096 mM) were added to bisADD-GNPs conjugates, aggregation appeared due to calcium-mediated aggregation (the TEM image of aggregation particle after addition of 0.081 mM Ca^{2+} is shown in image Fig. 1b). This result suggests that the bisADD on the surface of GNPs folded upon addition of Ca^{2+} with nano-Au aggregation.

The absorption and emission maxima of acridinedione dyes in acetonitrile solution are centered around 380 and 430 nm, respectively.[30,31] The peak at 380 nm is attributed to the intramolecular charge transfer (ICT) from nitrogen to carbonyl oxygen in the acridinedione moiety, and the emission at 430 nm to that of the local excited (LE) state. Absorption spectrum of bisADD **3** centered around 360 nm as shown in Figure S1 (see in Supplementary data) and the absorption spectrum of BisADD-GNPs **4** (Fig. S2) consist of two bands: (i) the additive absorption spectrum of bisADD due to ICT around 360 nm and (ii) a broad band in the visible region around 529 nm, which is attributed to the surface plasmon reso-

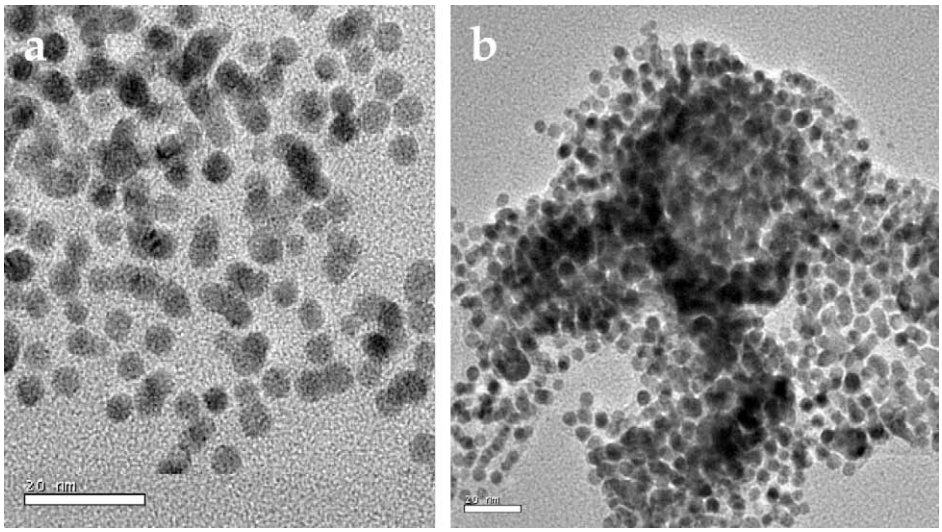


Figure 1. HR-TEM micrographs of bisADD-functionalized gold nanoparticles (a) before and (b) after addition of (9.6×10^{-5} M) Ca^{2+} ion to a bisADD-GNPs solution. (a) Spherical shape gold nanoparticles attachment with bisADD. (b) Aggregation in response to addition of Ca^{2+}.

nance (SPR) for the stabilized gold nanoparticles. Addition of Ca^{2+} to the acetonitrile solution of **4** (2.5×10^{-5} M) showed a red shift in the absorption maximum (Fig. 2). The significant change in the color visible to the naked eye (Fig. 3) demonstrates that the bis-ADD-GNPs recognize Ca^{2+} and lead to the nano aggregation. The absorption maximum of acridinedione remained unchanged on Ca^{2+} addition. The above changes indicate that the added Ca^{2+} brings the aggregation of bisADD-GNPs without any direct interaction with the chromophore. In contrast, the addition of other metal ions like Na^+, K^+, and Mg^{2+} did not show any variation in the absorption properties of **4** (Fig. S3).

Excitation of **4** at its absorption maximum, shows a weak emission with the quantum yield of 0.11 (±0.01), which is attributed to the PET process from the electron rich $-OCH_3$ to the relatively electron deficient excited state of the acridinedione fluorophore. Addition of Ca^{2+} to **4** shows a fluorescence enhancement without any spectral shift, as shown in Figure 4. An increase in the fluorescence intensity of **4** on addition of Ca^{2+} is attributed to the suppression of PET process. Whereas, the addition of other metal ions, such as Na^+, K^+, and Mg^{2+} showed only marginal (Figs. S4–S6) changes when compared to those with Ca^{2+}. These observations reveal the unique ability of **4** to detect Ca^{2+} ions selectively, which is evident from Figure 5. Addition of Ca^{2+} induced folding of the bichromophore, and the Ca^{2+} ions became nestled within the oxyethylene moiety

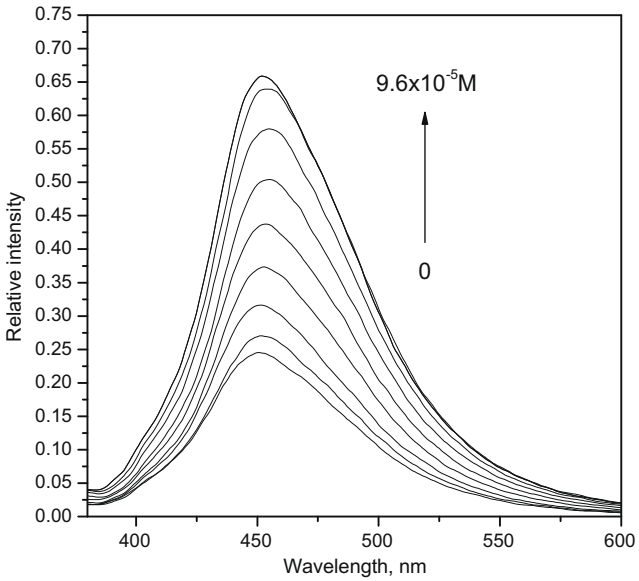


Figure 4. The emission (λ_{ex} = 360 nm) spectra of **4** upon addition of Ca^{2+} (0–9.6×10^{-5} M) in acetonitrile.

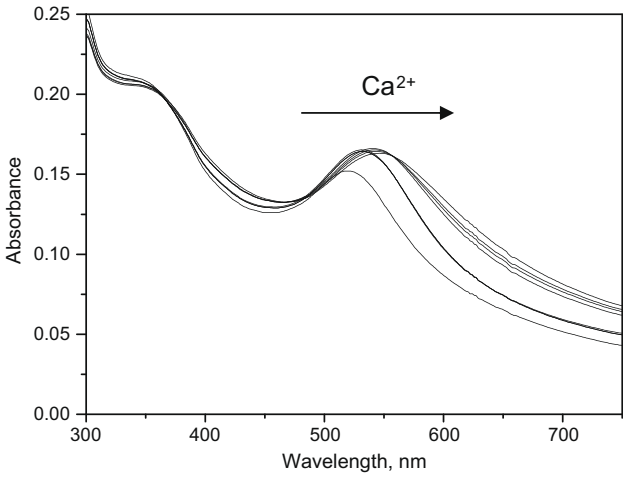


Figure 2. UV–visible spectra obtained of **4** upon addition of Ca^{2+} (0–9.6×10^{-5} M) in acetonitrile.

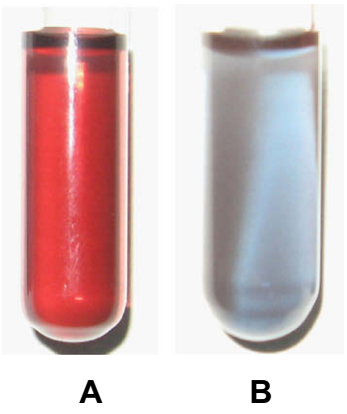


Figure 3. Photographs of (A) free bisADD-GNPs and (B) bisADD-GNPs with Ca^{2+} (9.6×10^{-5} M).

and the OCH_3 groups,[27] as shown in Scheme 2. This binding suppresses the PET process and also results in the rigidification of the host molecular framework, which in turn results in the fluorescence enhancement. Even though bisADD-GNPs and bisADD have similar fluorescence properties, the former is useful in colorimetric studies.

The complexation was established as 1:1 equilibrium from the Benesi–Hildebrand plot (Fig. S7). Moreover, it is also reversible in nature, which was confirmed by the addition of EDTA to bisADD-GNPs-Ca^{2+} complex. Complete reversal of the plasmon absorption band to the initial position was observed upon the addition of 95 μM EDTA to nanoparticle solution containing 85 μM Ca^{2+} (Fig. S8). Fluorescence spectrum also shows a decrease in the fluorescence intensity to the initial value of bisADD-GNPs upon the addition of EDTA to bisADD-GNPs-Ca^{2+} (Fig. S9). The selectivity

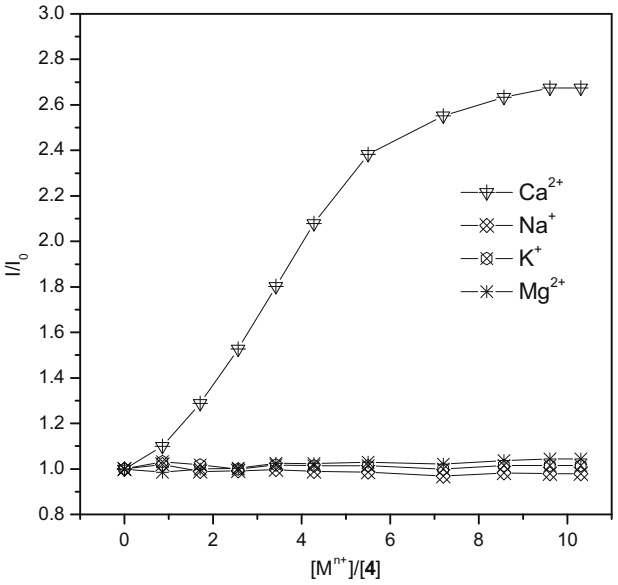
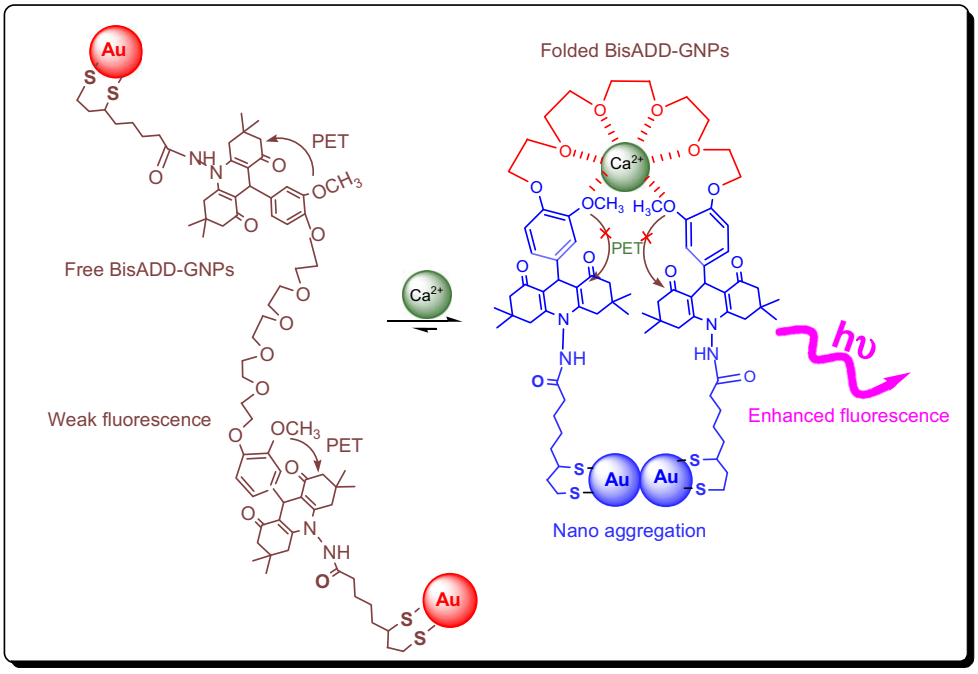


Figure 5. Plot of I/I_0 versus the ratio of metal ion: **4**, which illustrates the selectivity for Ca^{2+},over Na^+, K^+ and Mg^{2+} ions.



Scheme 2. The possible mechanism of the phenomenon of binding of the free bisADD-GNPs with Ca^{2+}.

of the Ca^{2+} sensing is proved by the addition of Ca^{2+} to bisADD-GNPs in the presence of other interfering metal cations (such as Na^{+}, K^{+}, Mg^{2+}, Ba^{2+}, and Sr^{2+}), which shows similar red shift in the absorption spectrum as observed with Ca^{2+} addition to bis-ADD-GNPs in absence of above interfering metal ions (Fig. S10). It is also found that the same fluorescence enhancement is observed in both the cases (Fig. S11).

In summary, we have demonstrated that bisADD-functionalized gold nanoparticles exhibit Ca^{2+}-induced folding of the bichromophore-GNPs, resulting in a color change from red to blue. This red shifted surface plasmon resonance (SPR) is due to aggregation of nanoparticles by the foldamer complexation, which was confirmed by TEM studies. Binding of Ca^{2+} at the oxyethylene moiety and $-OCH_3$ groups results in PET suppression, which leads to fluorescence enhancement.

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Supplementary data

Supplementary data (detailed synthetic procedures, characterization, 1H NMR data, FT-IR, HR-TEM images and photophysical studies of compound 4 with other metal ions) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.04.023.

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